



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/723,316	11/28/2000	Daniel Dupret	746220-0005(58763.000004)	6162

7590 07/02/2004

Robert M. Schulman
HUNTON & WILLIAMS
1900 K Street NW Suite 1200
Washington, DC 20006-1109

EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
----------	--------------

1637

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/723,316

Applicant(s)

DUPRET ET AL.

Examiner

Suryaprabha Chunduru

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 81-107 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 81-107 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' response to the office action and amendment filed on December 30, 2003, has been entered and considered.
2. Claims 1-80 are canceled and claims 81-107 are pending.

Response to arguments

3. Applicants' response to the office action is fully considered and found persuasive in part.
4. With reference to the objections made in the previous office action, Applicants' arguments and amendment are fully considered and the objections are withdrawn herein.
5. With reference to the rejection made in the previous office action under 35 USC 112, second paragraph applicants' arguments and amendment are fully considered and the rejection is withdrawn in view of the amendment.
6. With reference to the rejection made in the previous office action under 35 USC 102(e), applicants' arguments and amendment are fully considered and the rejection is withdrawn in view of cancellation of claims 1-13, 15, 17-29, and 31-39 by the amendment.
7. With reference to the rejection made in the previous office action under 35 USC 103(a), applicants' arguments and amendment are fully considered and the rejection is withdrawn in view of the cancellation of the claims 14 and 16 by the amendment.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 83-84, 107 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As MPEP 2163.06 notes “If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)”.

Here, the new limitation of “wherein any polymerase used in the method is used only to amplify or increase the number of copies of” in the claims 83-84, 107 appears to represent new matter. A careful review by examiner of the specification, this phrase was not present, Thus the phrase lacks descriptive support in the specification.

Since no basis has been found to support the new claim limitation in the specification, the claims are rejected as incorporating new matter.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 81-107 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims recite “assembly template”, which is unclear and indefinite because the assembly template is not defined in the instant specification and it is not clear whether it refers to an assembly matrix (solid support on which the hybridization of the fragments occur) or does it refer to a nucleic acid template. Thus the meets and bounds of the claims are not clear.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

A. Claims 81, 83-92, 97-105 are rejected under 35 U.S.C. 102(e) as being anticipated by Stemmer et al. (USPN. 6, 117, 679).

The following rejection is reinstated because the broad scope of new claim 81 and 107, do not exclude a DNA polymerase in the method steps.

Stemmer et al. teach a method of claim 81, of in vitro recombination, comprising (i) providing oligonucleotide cleavage fragments (see column 7, line 5-11, column 85, lines 4-20);

Hybridizing the cleavage fragments to an assembly template (random oligonucleotide) (column 7, line 11-22, column 85, lines 21-54)

Denaturing the ligated fragments and repeating denaturing and ligation steps multiple times to form a recombinant polynucleotide (see column 7, line 22-24, column 85, lines 60-67, column 86, line 1-10);

Stemmer et al. also teach said method comprises cleavage fragments derived from different polynucleotides (see column 5, line 38-52);

With regard to claims 83-84, Stemmer et al. teach that the polymerase can be used in amplifying or increasing the number of different polynucleotides, cleavage fragments, formed recombinant polynucleotide (see column 72, line 3-13, line 66-67, column 73, line 1-7);

With regard to claim 85, Stemmer et al. teach said recombinant polynucleotide formed possess new and advantageous properties (column 5, line 58-62);

With regard to claim 86, Stemmer et al. teach said hybridization and ligating steps are carried out simultaneously (see column 72, lines 57-65);

With regard to claims 87-89, Stemmer et al. teach said cleavage fragments are obtained by random cleavage using DNase I (see column 23, line 24-26);

With regard to claims 90-92, Stemmer et al. teach said cleavage fragments are obtained by using one or more restriction enzymes (see column 23, line 30-33);

With regard to claim 97, Stemmer et al. teach addition of additional assembly templates (more than one oligonucleotide templates) before formation of the recombinant polynucleotide (see column 85, line 61-67, column 86, line 1-10);

With regard to claim 98, Stemmer et al. teach that one or more cleavage fragments serve as the assembly template (column 5, line 19-51);

With regard to claim 99, Stemmer et al. also teach that said different polynucleotides or the cleavage fragments derived therefrom are double-stranded and be denatured before the hybridization step (see column 24, line 8-12);

With regard to claim 100, Stemmer et al. teach that said method further comprises selecting the formed recombinant polynucleotide that possess advantageous properties compared to a reference sequence (See column 4, lines 38-41, column 5, lines 1-18);

With regard to claim 101, Stemmer et al. teach the t the method further comprises cloning of the formed recombinant polynucleotide (see column 6, line 11-15, column 73, line 12-18);

With regard to claim 102, Stemmer et al. teach that said assembly template comprises oligonucleotides (see column 85, lines 21-33) that are complementary to the 3' and 5' ends of plurality of cleavage fragments (see column 86, lines 64-67, column 87, line 1-4);

With regard to claims 103-104, Stemmer et al. teach that said different polynucleotides have substantial portion of homology to each other and to the assembly template (see column 22, line 66-67, column 23, line 1-11);

With regard to claim 105, Stemmer et al. teach that said polynucleotides comprise artificial (synthetic) polynucleotides (see column 23, lines 42-46).

Thus the disclosure of Stemmer et al. meets the limitations in the instant claims.

B. Claims 81-83, 87-90, 97, 102-104, 106, are rejected under 35 U.S.C. 102(a) as being anticipated by Pachuk et al. (WO 97/42330).

Pachuk et al. teach a ligase-mediated method of claim 81-82, 106 , of in vitro recombination comprising

- (i) providing DNA fragments derived from different polynucleotide library (see page 4, lines 3-16, page 7, line 28);
 - (ii) hybridizing the cleavage fragments to an assembly template (see page 7, line 28-36, page 8, line 1-3);
 - (iii) ligating together the hybridized fragments that have adjacent ends with a ligase (see page 7, line 28-36, page 8, line 1-11);
 - (iv) denaturing the ligated fragments from the assembly template (see page 8, line 11-15);
- repeating at least the hybridizing, ligating and denaturing steps multiple times to form a recombinant polynucleotide comprised of the ligated fragments (see page 8, line 15-23).

With regard to claim 87-90, Pachuk et al. teach said cleavage fragments are obtained by cleavage with restriction enzymes, DNase digestion (page 4, line 11-16);

With regard to claim 97, Pachuk et al. teach that said method further comprises adding additional templates (see page 9, line 37, page 10, line 1);

With regard to claims 102-104, Pachuk et al. teach said assembly templates are oligonucleotides (see page 8, lines 34-35) complementary to the 3' and 5' ends of plurality of cleavage fragments (see page 8, line 35-37, page 9, line 1-20).

Thus the disclosure of Pachuk et al. meets the limitations in the instant claims.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 93-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pachuk et al. (WO 97/42330) in view of Harrington et al. (USPN. 5,874,283).

Pachuk et al. teach a ligase-mediated method of in vitro recombination comprising

- (i) providing DNA fragments derived from different polynucleotide library (see page 4, lines 3-16, page 7, line 28);
 - (ii) hybridizing the cleavage fragments to an assembly template (see page 7, line 28-36, page 8, line 1-3);
 - (iii) ligating together the hybridized fragments that have adjacent ends with a ligase (see page 7, line 28-36, page 8, line 1-11);
 - (iv) denaturing the ligated fragments from the assembly template (see page 8, line 11-15);
- repeating at least the hybridizing, ligating and denaturing steps multiple times to form a recombinant polynucleotide comprised of the ligated fragments (see page 8, line 15-23).

Pachuk et al. also teach said cleavage fragments are obtained by cleavage with restriction enzymes, DNase digestion (page 4, line 11-16); DNA ligase used is a thermostable ligase (with regard to claim 95) (see page 7, line 19).

However, Pachuk et al. did not teach adding degrading enzyme (FLAP endonuclease) to cut non-hybridized ends of the hybridized fragments.

Harrington et al. teach a mammalian FLAP endonuclease, wherein Harrington et al. disclose that the in the template-directed ligation and post-repair ligation models of DNA end-joining, wherein, base-pairing of several terminal nucleotides can result in the formation DNA flap structures, consists of unpaired single-strands (see column line 20-32); use of FEN-1, a FLAP endonuclease in DNA repair, recombination and replication involving cutting of DNA flap intermediates or DNA-RNA flap intermediates (see column 20, line 33-36, column 43, line 64-67, column 44, line 1-27).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method of ligase-mediated in vitro recombination as taught by Pachuk et al. with the method of adding FLAP endonuclease to cut the unpaired single-strands of ligated DNA molecules as taught by Harrington et al. to achieve an expected advantage of developing a sensitive and improved method of ligase-mediated in vitro recombination. An ordinary practitioner would have motivated to add of Flap endonuclease to the method of Pachuk et al. because addition of this limitation would remove non-hybridized ends or flap structures of the hybridized fragments and improve the specificity of the hybridized fragments by reducing non-specific background recombinants.

Conclusion

No claims are allowable.


Any inquiry concerning this communication or earlier communications from the

Art Unit: 1637

examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782 . The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Suryaprabha Chunduru
June 29, 2004


JEFFREY FREDMAN
PRIMARY EXAMINER
6/30/04